II. Remarks

A. Status of the claims

Claims 1, 2, 17, 18 and 19 have been amended without prejudice. It is respectfully submitted that support for the amendments can be found, e.g., on page 3, first paragraph, of the specification as filed and in the original claims.

Claims 1, 2 and 5-23 are pending. It is respectfully submitted that no new matter has been added by virtue of present amendments.

B. Rejection under 35 U.S.C. § 102

Claims 1, 2, 5-13, 16 18 and 20-23 were rejected under 35 U.S.C. § 102(b) over International Publication WO 90/04965 to Lee (hereafter "Lee").

The rejection is respectfully traversed.

Independent claims 1, 2, 17 and 18 and the claims dependent therefrom now recite that the composition is free of a non-permeant opioid antagonist. In contrast, the compositions disclosed in Lee comprise an abuse negating amount of at least one antagonist for said abusable substance in a form that is impermeable to the skin or mucosa to which it is applied (see claim 1). Accordingly, claims 1, 2, 17 and 18 and the claims dependent therefrom are now novel over Lee and withdrawal of the anticipation rejection is respectfully requested.

C. Rejections under 35 U.S.C. § 103

1. Lee in view of U.S. Patent No. 5,891,919 to Blum et al. and U.S. Patent No. 4,175,119 to Porter

Claims 1, 2, 5-13 and 15-23 were rejected under 35 U.S.C. §103(a) over Lee in view of U.S. Patent No. 5,891,919 to Blum et al. ("the Blum patent") and U.S. Patent No. 4,175,119 to Porter ("the Porter patent"). The Examiner stated that Lee "discloses a transdermal patch where an abusable opioid can be delivered and an opioid antagonist useful in deterring abuse is present in the patch yet is not permeable through the skin.

The antagonist causes nausea, vomiting and headaches when ingested orally." The Examiner relied on the Blum patent which, according to the Examiner, purportedly provides a substance which provides a bitter and/or spicy flavor for use as an aversive agent. The Examiner relied on Porter which, according to the Examiner, purportedly provides the use of an emetic to prevent accidental or intentional overdose of a psychoactive substance.

The rejection is respectfully traversed.

The Invention

The invention as recited in the presently amended claims provides for a composition where if misused, the abuser suffers a distressing effect in conjunction with the euphorigenic effect that results from the opioid analgesic. The concomitant occurrence of the distressing effect is intended to discourage, or act as a deterrent against, the abuser misusing the substance again. Significantly, the compositions of the present application do not act by preventing the euphorigenic effect, but rather by providing a distressing effect if the composition is misused (i.e., ingested orally, or administered as a bolus injection instead of transdermally).

To advance the prosecution of the claims and to further differentiate from the cited references, the claims have been amended to recite that the composition is free of a non-permeant opioid antagonist.

The Combination of References Does Not Provide All of the Limitations Of the Instant Claims

The Examiner's obviousness rejection appears to suggest that that Lee discloses a dosage form that comprises opioid analgesic and an opioid antagonist such as naloxone, which also causes side effects such as nausea, vomiting and headaches. From this platform, the Examiner's argument is that the skilled man would be motivated to add to the compositions disclosed in Lee, one or more of the other distressing agents disclosed in Blum or Porter. However independent claims 1, 2, 17 and 18 and the claims

dependent therefrom now recite that the composition does not comprise opioid antagonists. Accordingly, contrary to the Examiner's suggestion, a person having ordinary skill in the art would not arrive at the invention claimed by making the addition the Examiner suggests even if the cited references were properly combinable.

Lee purports a dosage form for the administration of an abusable substance by a transdermal route comprising abusable substance and at least one antagonist for the abusable substance (claim 1). Lee states at page 2, lines 32-33, that the antagonist is to "sufficiently negate the pharmacological effect of the abusable substance". This function is reiterated at page 4, lines 21-24 which states that "the antagonist for an abusable substance is a compound or composition which acts on the recipient to prevent or substantially diminish the pharmacological effects of the abusable substance or to substantially delay their manifestation". It is respectfully submitted that, these effects are achieved by the antagonist preventing binding of the agonist to its receptor.

Among the specific antagonists mentioned in Lee is naloxone, which the Examiner argues causes nausea, vomiting and headaches. These are known side effects of this antagonist. Nevertheless, the primary mechanism by which naloxone works is by being an opioid antagonist, which effectively prevents the abuser from achieving any euphorigenic effect. Therefore, it is respectfully submitted that the mechanism described in Lee is based on the fact that the antagonist blocks the agonist from binding to the abuser's receptors.

It is respectfully submitted that to arrive at the compositions and devices now claimed from the specification in Lee, a person having ordinary skill in the art would be required to replace (not add), the opioid antagonist with one of the distressing substances listed in claims 1, 2, 17 and 18 and the claims dependent therefrom. However, the cited references do not provide a reason or motivation for a person having ordinary skill in the art to make this modification. As discussed above, Lee teaches that it is critical its compositions comprise an opioid antagonist. Thus a person having ordinary skill in the

art looking to modify the dosage forms of Lee would only be motivated to substitute the antagonists it discloses with other opioid antagonists.

Nowhere is it suggested in Lee that a dosage form having reduced potential for abuse might be provided by including a compound which is a distressing substance as specified in the present claims. In fact, it is respectfully submitted that the mechanism described in Lee for reducing potential for abuse depends on the compound being an antagonist. Therefore, the mechanism and idea underlying Lee is entirely different to that of the current claims.

On this basis, it is respectfully submitted that a person having ordinary skill in the art would not replace the antagonists disclosed in Lee with any of the substances disclosed in Blum or Porter. None of the compounds disclosed in these references are opioid antagonists, and therefore it is respectfully submitted that the skilled artisan would not make the substitution necessary to arrive at the presently claimed invention. Importantly, none of the compounds disclosed in Blum or Porter are functionally equivalent to an opioid antagonist, which is part of the composition described in Lee.

Withdrawal of the obviousness rejection is respectfully requested.

2. Lee in view of U.S. Patent No. 46,001,390 and Drugs: Facts and Comparisons, entry for Pergolide Mesylate, pages 1621-1624

Claims 1, 2, 5-16, 18 and 20-23 were rejected under 35 U.S.C. § 103(a) over Lee in view of U.S. Patent No. 6,001,390 to Yum et al. ("the Yum patent") and Drugs:Facts and Comparison, entry for Pergolide Mesylate, pages 1621-1624 ("Drug Facts and Comparisons"). The Examiner relied on Yum which, according to the Examiner, purportedly describes pergolide salts and requires permeation enhancers for them to permeate through the skin. The Examiner relies on Drug Facts and Comparisons to demonstrate the side effects of pergolide. The Examiner concluded that since pergolides would not be permeable through the skin, they would act to deter misuse through injection or solvent distillation. The Examiner also concluded that "it would be obvious

to combine the teachings and formulations with an expected result of a transdermal formulation useful in treating pain without leading to potential abuse."

This rejection is respectfully traversed. As set forth above, Lee teaches that its compositions comprise an opioid antagonist. Therefore, a person having ordinary skill in the art looking to modify the dosage forms of Lee would only be motivated to substitute the antagonists it discloses with other opioid antagonists. Nowhere is it suggested in Lee that a dosage form having reduced potential for abuse might be provided by including a compound which is a distressing substance as specified in claims 1, 2, 17 and 18 and the claims dependent therefrom. Neither Yum nor Drug Facts and Comparisons in combination with Lee cure this deficiency. Accordingly, it is respectfully submitted that claims 1, 2, 5-16, 18 and 20-23 are not obvious over Lee in view of Yum and Drug Facts and Comparisons.

Withdrawal of the obviousness rejection is respectfully requested.

III. CONCLUSION

An early and favorable action is earnestly solicited. In view of currently recommended Patent Office policy, the Examiner is invited to contact the undersigned in the event that a telephonic interview would advance the prosecution of this application.

Respectfully submitted,
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